

Benefit of Tocilizumab for Severe Acute Respiratory Syndrome Coronavirus 2-Associated Heart Failure in Cytokine Release Syndrome Remains Unproven

Josef Finsterer

Klinik Landstrasse, Messerli Institute, Vienna, Austria

With interest, we read the article by Chitturi *et al.* about a 65-year-old female with coronavirus disease 2019 (COVID-19), treated with remdesivir and empiric antibiotics, and a history of diabetes, arterial hypertension, hyperlipidemia, transient ischemic attack (TIA), and breast carcinoma.^[1] The patient developed heart failure, multiorgan failure, and distributive shock 7 days after admission requiring mechanical ventilation and appropriate drug therapy.^[1] Shock therapy included norepinephrine, vasopressin, and steroids.^[1] Heart failure was treated with dobutamine and epoprostenol.^[1] In addition, she received a single dose of tocilizumab (400 mg). Under this regimen, the patient recovered. It was concluded that tocilizumab should be considered for the treatment of cardiogenic shock associated with COVID-19. We have the following comments and concerns.

The first shortcoming of the study is that the cause of shock and heart failure could not be identified. Myocarditis and pulmonary embolism were not appropriately excluded. A central nervous system disease such as encephalitis, stroke, sinus venous thrombosis, acute disseminated encephalomyelitis, and intracerebral bleeding was not excluded. Cerebral imaging had not been performed. Since the patient had a history of TIA and a high cardiovascular risk profile, it is crucial that ischemic stroke was excluded. Since COVID-19 goes along with hypercoagulability and increased frequency of thrombosis,^[2] it is crucial that pulmonary embolism or sinus venous thrombosis is appropriately excluded. Were there any indications for a patent foramen ovale? We should know if atrial fibrillation was ever recorded.

The second shortcoming is that the authors could not identify if the patient had experienced heart failure without takotsubo syndrome (TSS) or only TSS. TTS is usually

diagnosed upon the Mayo Clinic criteria and can be easily identified on transthoracic echocardiography. In addition, the electrocardiogram mimics myocardial infarction and creatine kinase (CK) is elevated. Unfortunately, CK values are not provided in Table 1. We should know if there any indications for TTS after revision of the echocardiographic recordings. Although there are various subtypes of TTS, the apical type prevails. Coronary artery stenosis was not excluded. Since the patient had a high cardiovascular risk profile, it is crucial to exclude myocardial infarction.

The third shortcoming is that no proof was provided for the assumption that tocilizumab had a beneficial effect on heart failure. Tocilizumab has several side effects, including arterial hypertension, hyperlipidemia, obesity, infections, bowel ulceration, and heart failure.^[3] Particularly in patients with pre-existing heart failure, tocilizumab can worsen systolic dysfunction.^[4] Thus, it is more likely that dobutamine and epoprostenol or the treatment for the cardiogenic shock rather than tocilizumab were responsible for resolution of heart failure.

Which is the reason why troponin-I further increased after the application of tocilizumab despite recovery from heart failure? Were there any other indications for myocardial infarction?

Overall, the interesting case does not convincingly show that tocilizumab can improve heart failure or systolic dysfunction. To confirm or exclude a beneficial effect of tocilizumab on heart failure, more appropriate study designs than a case report need to be applied. Since there are no indications that the cytokine storm triggers the development of heart failure, the pathophysiological concept that tocilizumab could be beneficial for heart failure should be abandoned.

Address for correspondence:

Josef Finsterer, Postfach 20, 1180 Vienna, Austria

© 2020 The Author(s). This open access article is distributed under a Creative Commons Attribution (CC-BY) 4.0 license.

AUTHOR'S CONTRIBUTION

JF: Design, literature search, discussion, first draft, and critical comments.

REFERENCES

1. Chitturi KR, Thacker S, Al-Saadi MA, Kassi M. Successful treatment of acute heart failure in COVID-19-induced cytokine storm with tocilizumab: A case report. *Eur Heart J Case Rep* 2020;4:1-6.
2. Mui LW, Lau JF, Lee HK. Thromboembolic complications of COVID-19. *Emerg Radiol* 2020:1-7.

3. Saito S, Okuyama A, Okada Y, Shibata A, Sakai R, Kurasawa T, *et al.* Tocilizumab monotherapy for large vessel vasculitis: Results of 104-week treatment of a prospective, single-centre, open study. *Rheumatology (Oxford)* 2020;59:1617-21.
4. Olejárová M. Adverse effects of biological therapy in rheumatology. *Vnitr Lek* 2016;62:605-12.

How to cite this article: Finsterer J. Benefit of Tocilizumab for Severe Acute Respiratory Syndrome Coronavirus 2-Associated Heart Failure in Cytokine Release Syndrome Remains Unproven. *J Clin Cardiol Diagn* 2020;3(2):1-2.